

## CLAIMS

What is claimed is:

- Sub C1
- 5 1. A method for altering angiogenesis in a mammal, comprising administering to the mammal, in a therapeutically effective quantity, a drug which alters binding or interaction of an artery-specific cell surface molecule with a vein-specific cell surface molecule in a therapeutically effective quantity.
- 10 2. The method of Claim 1 wherein the artery-specific cell surface molecule is an artery-specific ligand or receptor and the vein-specific cell surface molecule is a vein-specific receptor or ligand.
- 
- 15 3. The method of Claim 1 wherein the artery-specific cell surface molecule is an Ephrin family ligand and the vein-specific cell surface molecule is an Eph family receptor.
- 20 4. The method of Claim 3 wherein angiogenesis is inhibited and the drug interferes with binding or interaction of the artery-specific Ephrin family ligand with the vein-specific Eph family receptor.
- 
- Sub C2
- 25 5. The method of Claim 3 wherein angiogenesis is enhanced and the drug enhances binding or interaction of the artery-specific Ephrin family ligand with its vein-specific Eph family receptor.
- 
- Sub D11
- 25 6. The method of Claim 3 wherein the drug is an antagonist of the artery-specific Ephrin family ligand or an antagonist of the vein-specific Eph family receptor.

09085820-052890

- Sub  
cont'd*
7. The method of Claim 3 wherein the artery-specific Ephrin family ligand is EphrinB2 and the vein-specific Eph family receptor is EphB4.

- 5 8. A method for selectively delivering a drug to arteries in a mammal, comprising administering to the mammal a complex comprising:

- (a) the drug and  
(b) a component which binds an artery-specific cell surface molecule,

- 10 under conditions appropriate for the component of (b) to bind the artery-specific cell surface molecule, whereby the drug is delivered to arteries.

9. The method of Claim 8, wherein the artery-specific cell surface molecule is a ligand or receptor.

- 15 10. The method of Claim 8, wherein the artery-specific cell surface molecule is an Ephrin family ligand.

- Sub  
D12*
- 20 11. The method of Claim 10 wherein the drug is an anti-angiogenic drug and the component of (b) is an antibody specific for the artery-specific Ephrin family ligand, or a receptor of the artery-specific Ephrin family ligand.

12. The method of Claim 10 wherein the artery-specific Ephrin family ligand is EphrinB2.

- 25 13. The method of Claim 12 wherein the drug is an anti-angiogenic drug.

14. The method of Claim 12 wherein the drug is an angiogenic drug.

15. A method for selectively delivering a drug to veins in a mammal, comprising administering to the mammal a complex comprising:
- (a) the drug, and
- 5 (b) a component which binds a vein-specific cell surface molecule,
- under conditions appropriate for the component of (b) to bind the vein-specific cell surface molecule, whereby the drug is delivered to veins.
- 10 16. The method of Claim 15 wherein the vein-specific cell surface molecule is a receptor or ligand.
17. The method of Claim 15, wherein the vein-specific cell surface molecule is a vein-specific Eph family receptor.
- 15 18. The method of Claim 17 wherein the drug is an anti-angiogenic drug and the component of (b) is an antibody specific for the vein-specific Eph family receptor, or a ligand of the vein-specific Eph family receptor.
19. The method of Claim 17 wherein the vein-specific Eph
- 20 family receptor is EphB4.
20. The method of Claim 19 wherein the drug is an anti-angiogenic drug.
21. The method of Claim 19 wherein the drug is an angiogenic drug.
- 25 22. A transgenic mouse having an indicator gene which is detectably expressed in cells of arteries but not cells of veins.

09085800-052838

23. The mouse of Claim 22 wherein the indicator gene is inserted in an artery-specific Ephrin family ligand gene.
24. A transgenic mouse of genotype *EphrinB2*<sup>+/-</sup>.
25. A transgenic mouse in which EphrinB2 genes comprise an insertion that marks all arteries but not veins.
26. A transgenic mouse of genotype *EphrinB2*<sup>taulac2/+</sup>.
27. A method for identifying artery cells in a mouse having an indicator gene inserted in one or more alleles of *EphrinB2*, comprising staining a section of the mouse with a substance appropriate for detection of expression of the indicator gene.
28. A transgenic mouse having an indicator gene which is expressed in venous endothelial cells but not in arterial endothelial cells.
29. The mouse of Claim 28 wherein the indicator gene is inserted in a vein-specific Eph family receptor gene.
30. The transgenic mouse of Claim 29 wherein the vein-specific Eph family receptor gene encodes EphB4.
31. A transgenic mouse of genotype *EphB4*<sup>+/-</sup>.
32. A method for identifying vein cells in a mouse having an indicator gene inserted in one or more alleles of *EphB4*, comprising staining a section of the mouse with a substance appropriate for detection of expression of the indicator gene.

- 058350-058350
33. A method for testing an effect of a drug on growth of arteries, comprising administering the drug to a mouse having an indicator gene inserted in a gene specifically expressed in arteries, observing the effect of the drug, and comparing the effect to that produced in a suitable control mouse.
34. A method for testing an effect of a drug on growth of veins, comprising administering the drug to a mouse having an indicator gene inserted in a gene specifically expressed in veins, observing the effect of the drug, and comparing the effect to that produced in a suitable control mouse.
35. A method for identifying arterial endothelial cells in a tissue sample, comprising contacting the tissue sample with a molecule which binds to *EphrinB2*, wherein said molecule is linked to a label, and detecting the label, wherein if label is detected on a cell, the cell is an arterial endothelial cell.
36. The method of Claim 35, wherein said molecule is an antibody.
37. A method for identifying venous endothelial cells in a tissue sample, comprising contacting the tissue sample with a molecule which binds to *EphB4*, wherein said molecule is linked to a label, and detecting the label, wherein if label is detected on a cell, the cell is a venous endothelial cell.
38. The method of Claim 37, wherein said molecule is an antibody.

39. A method for directing a substance to arteries in a mammal, comprising administering to the mammal a complex which comprises the substance linked to a moiety which binds *EphrinB2*.
- 5 40. A method for directing a substance to veins in a mammal, comprising administering to the mammal a complex which comprises the substance linked to a moiety which binds *EphB4*.
- 10 41. A method for altering development of blood vessels in a mammal, comprising administering to the mammal a soluble polypeptide comprising the extracellular domain of an artery-specific cell surface protein or a soluble polypeptide comprising the extracellular domain of a vein-specific cell surface protein.
- 15 42. The method of Claim 41 wherein the artery-specific cell surface protein is an Ephrin family ligand and the vein-specific cell surface protein is an Eph family receptor.
- 20 43. The method of Claim 42 wherein the Ephrin family ligand is *EphrinB2* and the Eph family receptor is *EphB4*.
- 25 44. A method for identifying a drug that inhibits interaction of an arterial endothelial cell-specific surface molecule with a venous endothelial cell-specific surface molecule, comprising:
- (a) combining:
    - (1) the arterial endothelial cell-specific surface molecule;
    - (2) the venous endothelial cell-specific surface molecule; and

05085321 05085321 05085321

See  
DB

- 5 (3) a drug to be assessed for its ability to  
inhibit interaction between the molecule of  
(1) and the molecule of (2), under conditions  
appropriate for interaction between the  
molecule of (1) and the molecule of (2);
- (b) determining the extent to which the molecule of  
(1) and the molecule of (2) interact; and
- 10 (c) comparing the extent determined in (b) with the  
extent to which interaction of the molecule of (1)  
and the molecule of (2) occurs in the absence of  
the drug to be assessed and under the same  
conditions appropriate for interaction of the  
molecule of (1) with the molecule of (2);
- 15 wherein if the extent to which interaction of the  
molecule of (1) and the molecule of (2) is less in the  
presence of the drug than in the absence of the drug,  
the drug is one which inhibits interaction of the  
arterial endothelial cell-specific molecule of (1) with  
the venous endothelial cell-specific molecule of (2).
- 20 45. The method of Claim 44 wherein the arterial endothelial  
cell-specific surface molecule is an Ephrin family  
ligand and the venous endothelial cell-specific surface  
molecule is an Eph family receptor.
- 25 46. The method of Claim 45 wherein the Ephrin family ligand  
is EphrinB2 and the Eph family receptor is EphB4.
47. A method for identifying a drug that enhances  
interaction of an arterial endothelial cell-specific  
surface molecule with a venous endothelial cell-  
specific surface molecule, comprising:
- 30 (a) combining:







63. A cDNA library produced from isolated venous endothelial cells.
64. A method for identifying a gene which shows differential expression in venous endothelial cells compared to arterial endothelial cells, comprising producing a transgenic mouse having an indicator insertion gene in a gene to be tested for differential expression, and observing expression of the indicator insertion gene, wherein a difference in expression of the indicator insertion gene in venous endothelial cells and arterial endothelial cells indicates a gene which shows differential expression.
65. A method for modifying arteries in a mammal, comprising genetically altering isolated arterial endothelial cells and introducing the altered cells into the mammal.
66. A method for modifying veins in a mammal, comprising genetically altering isolated veins endothelial cells and introducing the altered cells into the mammal.